## REMARKS

Claims 1-31 were originally filed and are currently pending. Claims 22 and 31 are cancelled herein. Claims 1, 3, 10, 17, 18, 19, 20, 21, 27, 28 and 30 are amended herein as discussed in more detail below. Claims 32-39 are newly added. The amendments to the Claims and Specification are fully supported by the specification as originally filed and do not constitute new matter. Accordingly, entry of these amendments is respectfully requested.

Objection to the Abstract:

The Examiner has objected to the Abstract of the Disclosure. In particular, the Examiner contends that the Abstract "does not meet the requirement of the MPEP for U.S. application" and that correction is required under MPEP 608.01(b). Applicants respectfully traverse this objection. The Examiner has failed to specifically point out the defect in the Abstract that is required to be corrected. Applicants note that the instant application is a national stage application filed under 35 U.S.C. 371. Consequently, the Abstract of this application is not required to be on a separate sheet, preferably following the claims, as set forth in MPEP 608.01(b). In fact, the Abstract of this application is properly located on the front page of the Patent Cooperation Treaty publication. Applicant respectfully submit that the Patent Office and the public can quickly determine from the reading of this abstract the nature and gist of the technical disclosure of the application. However, in the interest of furthering the prosecution of this application, Applicants have cancelled the original Abstract, thereby rendering moot this objection with respect thereto, and replaced it with a new Abstract as set forth above. Applicants respectfully submit that this new Abstract fully meets the requirements of MPEP 608.01(b).

Rejection of Claims 30 and 31 under 35 U.S.C. 101:

The Examiner has rejected Claims 30 and 31 under 35 U.S.C. 101. In particular, the Examiner contends that the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process. In other words, the Examiner contends that Claims 30 and 31 are not "proper" process claims under 35 U.S.C. 101.

Applicants have cancelled Claim 31, thereby rendering moot this rejection with respect to this claim.

Applicants have amended Claim 30 to refer to a method for preparing a pharmaceutical composition comprising admixing a compound of formula (I) with one or more pharmaceutically acceptable carriers therefor. Applicants respectfully submit that amended Claim 30 is a proper process claim under 35 U.S.C. 101, and therefore respectfully request the withdrawal of the above rejection with respect thereto.

Objection to the Disclosure:

The Examiner has objected to the disclosure for failing to include the cross-reference to related applications.

Applicants have amended the Specification by inserting the required cross-reference to the International Application and to the Australian priority document. In view of this, Applicants respectfully request the withdrawal of this objection.

Rejection of Claims 1-31 under 35 U.S.C. 112, ¶ 1:

The Examiner has rejected Claims 1-31 under 35 U.S.C. 112, ¶ 1, for "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." In particular, the Examiner contends that:

> **. . . the written description of the invention within the disclosure is incomplete because the complete chemical identities of most of the specific exemplifications are not completely defined; see NMR/Mass Spec tables wherein compounds are identified by number only. The incomplete spectroscopic data supplied (mass spectral "$M^+$" data and some NMR data) does not overcome this problem.**

Applicants traverse this rejection for the following reasons.

The complete chemical identities of the exemplified compounds are provided in the Specification, particularly in Tables 1 to 8. These Tables set out the exact chemical structures of a multitude of compounds according to the invention, including those compounds

which are explicitly disclosed in Examples 1 to 18. This structural information is supplemented by NMR and/or MS data, as set forth in Tables 9 to 11, and activity data, as presented in Tables 12 to 14. Applicants respectfully point out that the numbering of the compounds is consistent throughout these Tables and Examples. For example, Compound No. 1 in Table 1 is the same compound as Compound No. 1 in Example 1 and Compound No. 1 in Table 12. Thus, when one skilled in the art considers the structural and physical characteristic data of the compounds listed in Tables 1 to 8 together with the description of their synthesis and use as provided in the Specification, one would reasonably conclude that the inventors had possession of the invention as set forth in Claims 1-31 at the time the instant application was filed.

In addition to the foregoing rejection, the Examiner rejected Claims 1-31 under 35 U.S.C. 112, ¶ 1, for lack of enablement. In particular, the Examiner contends that:

> **The scope of the instant claims as defined by claims 1-4, 12 and 23-29 is excessive because said claims encompass a subject matter area much greater than that supportable by the instant disclosure. This is due in part to the presence in the claims of incompletely defined and therefore open ended generic terms; e.g. at lines 4-5 wherein the term "optionally substituted" fails to be supported by definitions identifying the "substituents," and "heterocyclic radical" wherein the quantity(ies) and identity(ies) of heteroatoms(s) are not provided in the claim, etc. See also the definition of "Ar."**

Applicants have amended Claims 1, 27, 28 and 30 to specifically recite the quantity and identity of the heteroatoms in the heterocyclic radicals disclosed therein and to specifically list the optional substituents for the Het and Ar groups. Support for these amendments is found in the Specification on page 6, lines 17-20, and page 11, lines 14-17, respectively.

In addition, the Examiner rejected Claims 1-31 under 35 U.S.C. 112, ¶ 1, for lack of enablement. In citing the *In re Wands* factors, the Examiner particularly noted that:

**A. The subject matter breadth of claims 1-4, 12 and 23-29 is overly broad for the reasons noted in the rejection for excessive scope above.**

. . .

**F. The amount of direction provided by the inventor is limited to a partial disclosure of the specific embodiments prepared, a showing of how to make pharmaceutical compositions, a showing of how to inhibit rhinoviral strains *in vitro* with a substantial number of specific embodiments, but with no showing that the administration of any instant compound will "prevent" rhinoviral infection or development of said infection into disease in a mammalian host.**

**G. The existence of working examples is limited to the description of a few synthetic examples and a substantial number of biological testing examples. However, the latter examples are not complete because the identity of specific compounds is frequently unavailable because of incomplete identification of compounds synthesized as reported by the disclosure.**

**H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is therefore deemed to be excessive because the disclosure is incomplete in its identification of compounds prepared, and because the disclosure does not provide any factual basis in support of the allegation that compounds disclosed herein are effective to "prevent" infection or development of said infection into disease following exposure to a source of rhinovirus.**

Applicants traverse this rejection for the following reasons.

For the reasons set forth above, Applicants respectfully submit that the chemical identities of all the compounds disclosed in both the synthetic examples and the biological testing examples are easily determined by the structures provided in the Tables 1 to 8 in light of the fact that the numbering of the compounds in these Tables is the same as the numbering of the compounds in both the synthetic examples and the biological testing examples. Thus, the disclosure is complete in its identification of the compounds prepared and tested.

Applicants respectfully submit that it has been demonstrated in the prior art that capsid binding compounds have *in vivo* efficacy in preventing picornaviral infection. Given that the compounds of the present invention are structurally analogous to capsid binding compounds shown to have this prophylactic activity, and given that the presently claims compounds are

believed to interact with the same capsid binding pocket of picornavirus, one of ordinary skill in the art would reasonably expect the compounds of the invention to have *in vivo* efficacy in preventing picornaviral infection based on the results of the *in vitro* assays. Moreover, the comparative compounds, *i.e.*, Pirodavir and Pleconaril, included in Examples 13, 15, 16, 17 and 18 are capsid binding compounds which have been extensively studied *in vivo*, and have been shown to have efficacy in preventing picornaviral infection in mammalian hosts, including humans. See, for example, Hayden, F.G. *et al.*, "Safety and Efficacy of Intranasal Pirodavir (R77975) in Experimental Rhinovirus Infection," *Antimicrobial Agents and Chemotherapy* (1992), Vol. 36, pp. 727-732; and Schiff, G.M. *et al.*, "Clinical Activity of Pleconaril in an Experimentally Induced Coxsackie's A21 Respiratory Infection," *J. Infectious Diseases* (2000), Vol. 181, pp. 20-26. Furthermore, numerous review articles have also been published affirming the efficacy of capsid binding compounds *in vitro* and *in vivo* for treating and preventing rhinovirus and other related picornaviral diseases of mammalian hosts. See, for example, Arruda, E. *et al.*, "Clinical studies of antiviral agents for picornaviral infections" in *Antiviral Chemotherapy* (1995), Jeffries, D.J. and DeClercq, E. (eds), John Wiley & Sons Inc., Sussex, England; Rogers, J.M. *et al.*, "Pleconaril a broad spectrum antipicornavirus agents" in *Antiviral Chemotherapy* (1999), Mills *et al.* (ed), Kluwer Academic/Plenum Publishers, NY, USA; Rotbart, H.A. *et al.*, "Treatment of human enterovirus infections" in *Antiviral Research* (1998), Vol. 38, pp. 1-14; and Andries, K., "Discovery of pirodavir, a broad-spectrum inhibitor of rhinoviruses" in *The Search for Antiviral Drugs*, Adams, J. *et al.* (eds), Berhauser, Boston, USA. Copies of the foregoing references are submitted herewith in a Supplemental Information Disclosure Statement.

In light of the large body of art correlating capsid binding compounds to the treatment and prevention of picornaviral infections, and in light of the complete and full description in the Specification of the synthesis and testing of the compounds of the invention, Applicants respectfully submit that the disclosure of the Specification clearly enables one skilled in the art to make and use the invention as set forth in Claims 1-31 with minimum experimentation and a reasonable expectation of success. Applicants further note that Examiner has not provided any evidence to suggest that the compounds of the invention would **not** be

useful in treating or preventing picornaviral infection, as required in setting forth a rejection of enablement under 35 U.S.C. 112, ¶ 2.

Accordingly, Applicants respectfully request the withdrawal of all of the above rejections of Claims 1-31 under 35 U.S.C. 112, ¶ 1.

Rejection of Claims 1, 3, 17-22, 27-28 and 30 under 35 U.S.C. 112, ¶ 2:

Claims 1, 3, 17-22, 27-28 and 30 are rejected under 35 U.S.C. §112, ¶ 2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner contends that:

> **In claim 1 the terms "optionally substituted" (lines 4-5 and definition of "Ar") and "heterocyclic radical" (lines 4-5) are indefinite because the optional substituents have not been defined in the claim and because the quantity(ies) and identity(ies) of heteroatom(s) have not been identified in the claim. See also claims 27, 28 and 30.**
>
> **In claim 3, the term "Y is as defined above" renders the claim incomplete because "Y" is not defined in claim 1 (but is defined in claim 2).**
>
> **In claim 10 the term "alkylene" appears to be technically incorrect in view of the dictionary definition in the McGraw-Hill Dictionary of Chemistry (1997, p. 14) which definition requires that the noted term be a monoradical of an alkene. Examiner suggests substitution of the term – alkyl diradical – for the noted term. See also claims 1 (2x), 17-21 (2x), 28 (2x) and 30 (2x).**
>
> **Claim 22 is incomplete because it does not completely define the subject matter being claimed within the claim. Applicant is respectfully requested to substitute reference to the disclosure with a complete recitation of the subject matter being referred to within the noted claim. Note that the question of completeness of the "Table" incorporated subject matter has been raised in other rejections supra.**

As noted above, Applicants have amended Claims 1, 27, 28 and 30 to specifically recite the optional substituents for Ar and heterocyclic radicals and to specify the quantity and identity of the heteroatoms present in the heterocyclic radicals.

Applicants have also amended Claim 3 to be dependent upon Claim 2 (instead of Claim 1).

Applicants disagree, however, with the Examiner's reasons for rejecting the use of the term "alkylene". It is Applicants' understanding that the term "alkylene" can refer generically to a divalent alkyl radical and the term has been correctly used as such in the Specification and Claims. In fact, the term "alkylene" is defined in Chambers Science and Technology Dictionary as a "general term for divalent hydrocarbon radicals." Furthermore, the fact that the term "alkylene" as used in the Specification and Claims is meant to be divalent is clearly evident from formula I which shows the group "-Alk-" as a divalent group. Even if the term "alkylene" did have an alternative meaning as indicated in the dictionary referred to by the Examiner, we believe that it is clear that this meaning is not applicable in the present case. Applicants respectfully submit that the Examiner would concede that the term "methylene" is a subset of "alkylene" and that the divalent group $-CH_2-$ is a methylene group. However, in the interest of furthering this application to allowance, Applicants have amended Claims 1, 10, 17, 18, 19, 20, 21, 27, 28, 30 to replace the term "$C_{x-y}$alkylene" with "divalent $C_{x-y}$alkyl" (where x and y are as originally defined in the claim) at each occurrence.

Applicants have cancelled Claim 22 and added new Claims 32-39 to specifically recite by name the compounds listed in Tables 1 to 8 in the Specification. In particular, Claim 32 is directed to the compounds listed in Table 1; Claim 33 is directed to the compounds listed in Table 2; Claim 34 is directed to the compounds listed in Table 3; Claim 35 is directed to the compounds listed in Table 4; Claim 36 is directed to the compounds listed in Table 5; Claim 37 is directed to the compounds listed in Table 6; Claim 38 is directed to the compounds listed in Table 7; and Claim 39 is directed to the compounds listed in Table 8. These names are inherent in the structures provided in Tables 1 to 8 in that one skilled in the organic chemistry art could easily obtain the chemical name of each of these compounds based on the particular chemical formulae given and the particular choices for the various substituents. Accordingly, the addition of these new Claims does not constitute the addition of new matter, but instead, merely provides the inherently disclosed names of the compounds indicated in Tables 1 to 8.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the above rejections of Claims 1, 3, 17-21, 27-28 and 30 under 35 U.S.C. 112, ¶ 2, are now

overcome. Furthermore, Applicants respectfully submit that new Claims 32-39 are patentable under 35 U.S.C. 101 and 112.

Rejection of Claims 1, 3-4, 8, 10-16, 23-27 and 30-31 under 35 U.S.C. 102(b):

Claims 1, 3-4, 8, 10-16, 23-27 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Stetter et al. (U.S. Patent No. 4,472,416). In particular, the Examiner contends that the compounds disclosed in the Stetter et al. "read on the instant noted claims including those directed to compounds, pharmaceutical compositions and "use" as a fungicide on plants." The Examiner also noted that EP 0 290 906 (Bayer I) appears to be an equivalent of the Stetter et al. and that EP 0 248 253 (Bayer II) appears to anticipate only the compound and composition claims.

Applicants traverse this rejection for the following reasons:

Applicants respectfully submit that the references do not anticipate any of the claims of the present application. Although the references describe compounds having oxime ether substituted aryl groups linked to heterocyclic radicals, the groups linking the heterocyclic radicals to the aryl groups do not satisfy the limitations of formula I. In this regard, formula I specifically requires the heterocyclic radical to be linked to the aryl radical via a "-A-Alk-W-" linking group. Since none of the choices for A, Alk and W can be a **substituted** methylene group or, for that matter, any other **substituted** carbon group, the compounds disclosed in the cited references, which do require a substituted methylene group or another substituted carbon group, cannot be considered to fall within the scope of formula I. Accordingly, Applicants respectfully submit that Claims 1, 3-4, 8, 10-16, 23-27 and 30-31 are not anticipated under 35 U.S.C. 102(b) by the disclosures of Stetter et al. and Bayer II.

Conclusion:

Applicants respectfully submit that all objections and rejections of the claims herein are hereby overcome or rendered moot by the amendments to the Claims and Specification as set forth above. Accordingly, Applicants respectfully submit that all claims

remaining in the application are allowable and favorable consideration with respect thereto is earnestly requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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